

**REMARKS**

The claims have been amended to more clearly describe the subject matter of the invention.

Claims 6, 11, 22, 26, 32 and 37-39 have been cancelled.

Claim 2 and 18 have been amended by inserting the antiviral "foscarnet," which was particularly recited in dependent claim 5 that initially depended from now cancelled original claim 1. Support can also be found in the Specification in Tables 2-4.

Claims 2 and 18 have been amended by inserting "9-[4-hydroxy-2-(hydroxymethyl)butyl]guanine" which is the formal name for the antiviral H2G. Support for this amendment can be found in the Specification at column 3, lines 66-67.

Claims 2 and 18 have also been amended by inserting the terms "active" and "ingredient." Support for this amendment can be found in the Specification at column 5, lines 19-20.

Claims 2, 4, 18 and 20 have been amended to recite particular antivirals and/or glucocorticoids and to define "synergistic". Support for the definition of "synergistic" can be found throughout the application, but in particular at column 6, lines 28-36, column 10, lines 54-63 and Figures 1-2.

Claims 2, 18 and 24 have also been amended by incorporating the limitation of "recurrent herpes virus infection" found in claims 26 and 32.

Claims 16, 24, 27, 29 and 31 have been amended to correct dependencies in view of the canceled claims.

Claims 8-10 and 13-15 have been amended to harmonize the dependent claims with the transitional phrase "consisting essentially of" found in claim 2.

No new matter has been added.

**Rejections Under 35 U.S.C. § 112, first paragraph**

In the Office Action issued March 4, 2005, the Examiner rejected claims 1, 3 and 16-40 for lack of enablement. In the Amendment filed July 13, 2005, Applicants canceled claims 1, 3, 17 and 19. Applicants also amended claims 8 and 24, deleting reference to "prophylaxis" and inserting the language suggested by the Examiner.

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In this Supplemental Amendment, submitted for the sole purpose of expediting prosecution and without disclaimer of unclaimed subject matter, Applicants have restricted the claims to specific antiviral substances and particular glucocorticoids. Applicants have also amended the claims to better define the term "synergistic." In support of "synergistic combination" and "synergistic dose," Applicants offer the following comments.

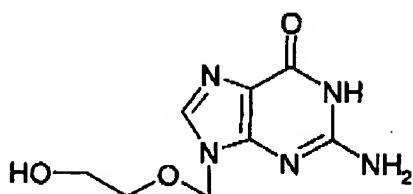
Applicants have submitted a manuscript entitled "ME-609: A treatment for recurrent herpes simplex virus infections" which summarizes the preclinical and early clinical experience of ME-609, a composition containing 5% acyclovir and 1% hydrocortisone. As discussed on pages 14-18 and in Table 2, the combination of acyclovir and hydrocortisone showed improved efficacy as compared to acyclovir or hydrocortisone alone. The Harmenberg et al. (2003, *Antiviral Chemistry & Chemotherapy* 14:205-215) and Evans et al. (2002, *Antimicrobial Agents and Chemotherapy* 46:1870-1874) references reiterate these results.

The results obtained for the acyclovir and hydrocortisone combination are similar to those reported for the combination of foscarnet and hydrocortisone (see Harmenberg et al. manuscript page 15, lines 21-22 and page 18, lines 3-5 as well as the instant Specification, Tables 2-4 and Figure 3).

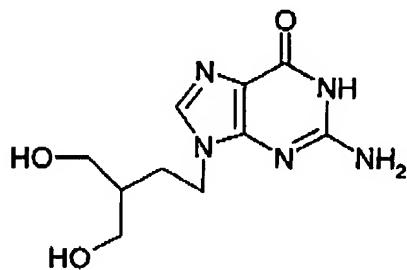
Applicants note that acyclovir, penciclovir and H2G (i.e. 9-[4-hydroxy-2-(hydroxymethyl)butyl]guanine) have a very close structural and functional resemblance as shown below.

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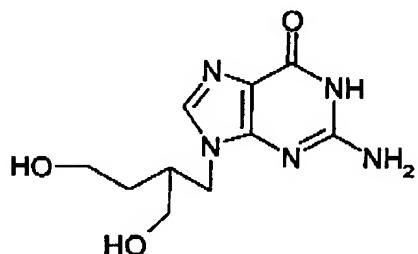
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acyclovir



penciclovir



9-(4-hydroxy-2-(hydroxymethyl)butyl)guanine

Based on the close structural and functional similarity between acyclovir, penciclovir and H2G, penciclovir and H2G are fully expected to have an efficacy similar to that of acyclovir when used as a treatment for herpes simplex virus infections. As a matter of interest, Applicants point out that 9-[4-hydroxy-2-(hydroxymethyl)butyl]guanine has the trivial name of "H2G," but has recently been awarded the official INN (international non-proprietary nomenclature) name "omaciclovir."

Similarly, hydrocortisone and its esters are closely related both structurally and functionally and are thus fully expected to perform similarly.

### Rejections Under 35 U.S.C. § 103

The Examiner rejected claims 1-4, 7, 13-21 and 23-40 as obvious over Levin (USP 5,656,301), claims 1-5, 7-10, 13-21 and 23-40 as obvious over Smith (USP 4,902,678) in view of Underwood (USP 3,317,384) and claims 6, 11, 12 and 22 as being obvious over Smith in combination with Underwood and Chemical Abstract 103:172328.

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Applicants addressed these rejections in the Amendment filed July 13, 2005. To summarize, even though Levin's Examples 20, 32 and 43 discuss acyclovir and hydrocortisone or an ester, the instant invention is still distinguishable. Specifically, the instant claims recite the transitional phrase "consisting essentially of" and are limited to active ingredients consisting of at least one particular antiviral and at least one particular glucocorticoid. Levin's invention is the combination of the active ingredient LYCD and an additional medicinal agent. That is, LYCD is a required active ingredient. The instant claims are limited to particular antiviral and glucocorticoid active ingredients and so exclude LYCD which is not a member of the recited antiviral or glucocorticoid active ingredient groups. Moreover, as stated by Dr. Spruance in his Declaration, a skilled artisan would not have a reasonable expectation of success for combinations of the antivirals and glucocorticoids disclosed in Levin's Examples without LYCD being present.

Likewise, with respect to Smith and Underwood, with or without Chemical Abstract 103:172328, and again as stated by Dr. Spruance in his Declaration, a skilled artisan would not have a reasonable expectation of success and would furthermore lack the motivation to combine these two references in the first place.

### Conclusion

In view of the above remarks, all the claims remaining in the case as amended, including newly added claims, are submitted as defining non-obvious, patentable subject matter. Reconsideration of the rejections and allowance of the claims are respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leonard R. Svensson (Reg. No. 30,330) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

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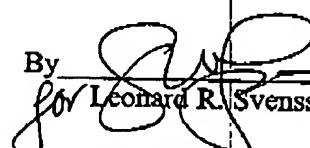
If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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LRS/SWG  
1718-0214P

Attachment(s): PTO 1449

Harmenberg manuscript "ME-609: A treatment for recurrent herpes simplex virus infections."

Harmenberg et al. (2003) *Antiviral Chemistry & Chemotherapy* 14:205-215.

Evans et al. (2002) *Antimicrobial Agents and Chemotherapy* 46:1870-1874.

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